IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dipak K. Banerjee, et al.

Appln. No.: 09/779,447

Filed: February 9, 2001

For: METHODS FOR INHIBITING ANGIOGENESIS

CERTIFICATE OF FACSIMILE TRANSMISSION

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

I hereby certify that the attached correspondence including:

- Informative Motion (2 pages)
- Appeal Brief (9 pages)

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April 11, 2006 By: _____
Heath W. Hoglund

UPR-0100

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dipak K. Banerjee, et al.	Group Art Unit: 1623
Appln. No.: 09/779,447	Examiner: Howard V. Owens, Jr.
Filed: February 9, 2001	
For: METHODS FOR INHIBITING ANGIOGENESIS	INFORMATIVE RESPONSE

To: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir or Madam:

An appeal in this case was returned by the Board to the Examiner because the Appeal Brief did not comply with the new rules set forth in 37 C.F.R. § 41.37. The case was specifically remanded to the Examiner to issue an Office Action requiring a substitute Appeal Brief. Although the Examiner has not yet issued such notice, applicants respectfully submit herewith a substitute Appeal Brief. Applicants respectfully request the entry of this substitute Appeal Brief and that the Examiner issue a revised Examiner's Answer in compliance with the Board's Order.

Respectfully submitted,

April 11, 2006

By: _____

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant: Dipak K. Banerjee, *et al.*	Group Art Unit: 1623
Application. Number: 09/779,447	Examiner: Howard V. Owens, Jr.
Filed: February 9, 2001	
For: METHODS FOR INHIBITING ANGIOGENESIS	**APPEAL BRIEF**

This is an appeal from the Office Action dated May 17, 2004 (Paper 15), which finally rejected claims 9, 14 and 18.

I. Real Party in Interest.

The University of Puerto Rico is the assignee and owner of the patent application and the real party in interest.

II. Related Appeals and Interferences.

There are no related other appeals or interferences known to appellants which will directly affect or be directly affected by or have a bearing on the Boards decision in this appeal.

III. Status of the Claims.

Claims 1-8, 10-13, 15-17 and 19-92 have been cancelled.

Claims 9, 14 and 18 have been rejected by the examiner under 35 U.S.C. §103 as being unpatentable over Banerjee, *et al.*, *Is asparagine-linked protein glycosylation an obligatory requirement for angiogenesis?*, Indian J. Biochem. and Biophysics, Vol. 30(6),

pp.389-94 (1993) (hereinafter "Banerjee 1993") and Tiganis, *et al., Functional and Morphological Changes Induced by Tunicamycin in Dividing and Confluent Endothelial Cells*, Exp. Cell Research, Vol. 198, pp. 191-200 (1992) (hereinafter "Tiganis 1992").

IV. Status of Amendments.

After the final rejection, applicants requested entry of amendments to claims 9 and 14 so that these claims would stand in independent form. Applicants further requested cancellation of claims 2-8, 10-13, 15-17 and 19-92, without prejudice. These amendments were entered.

V. Summary of Claimed Subject Matter.

The invention relates to the inhibition of angiogenesis in a patient, which is useful in the treatment of diabetic retinopathy, atherosclerotic plaques, scleroderma, hypertrophic scarring, vascular adhesions, angiofibroma, trachoma graft neovascularization, corneal graft neovascularization, neovascular glaucoma, thrombosis, restenosis, osteoporosis, macular degeneration, arthritis, hemangiomas, psoriasis and tumors. (Specification p. 31, lines 2-5.) More specifically, the invention relates to the safe administration of tunicamycin to patients for this purpose. (Specification p. 27, lines 1-3.)

A. Background of the Invention.

Over seven years prior to filing the patent application which is the subject of this appeal, Prof. Dipak K. Banerjee (one of the inventors) published the article titled *Is asparagines-linked protein glycosylation an obligatory requirement for angiogenesis?* (again, "Banerjee 1993"). This article investigated the basic, biologic link between glycosylation and angiogenesis. Through *in vitro* studies, Banerjee 1993 concluded that these two

processes are linked. Among other experimental data, Banerjee 1993 disclosed that tunicamycin inhibited glycosylation.

Banerjee 1993, however, was limited to *in vitro* studies and did not take the further step of attempting (or even suggesting) to inhibit angiogenesis in a patient by administration of tunicamycin. The subject article neither taught nor suggested that tunicamycin (nor any of the other compounds used in the disclosed experiments) could be administered *in vivo*, let alone in human patients, to treat angiogenesis.

Although, as the examiner appears to concede, Banerjee 1993 did not extend its teachings to *in vivo* applications and did not attempt to inhibit angiogenesis in a patient by the administration of tunicamycin, the examiner further relies upon a contemporaneous article titled *Functional and Morphological Changes Induced by Tunicamycin in Dividing and Confluent Endothelial Cells* (again "Tiganis 1992"). This article investigated the effect of tunicamycin on endothelial cells. As with Banerjee 1993, Tiganis 1992 disclosed experiments that were conducted *in vitro*. Regarding the possible extension of the disclosed experiments to *in vivo* applications, Tiganis 1992 expressly warned that such an application would cause "damage to brain microvessels in tunicamycin-treated animals." (Tiganis 1992, p. 199.) Tiganis 1992, therefore, is fairly viewed for the teaching that tunicamycin could not be administered to human patients to inhibit angiogenesis for the obvious reason that brain damage would be an unacceptable side effect.

B. Claimed Aspects of the Invention.

Against the above teaching, which would prevent administering tunicamycin to a human patient for fear of causing brain damage, the subject patent application demonstrates that tunicamycin can be administered for the treatment of angiogenesis-related diseases. The precise dosage regime is explained in detail in the specification. (Specification p. 48, line 19

– p. 49, line 27.) And, this invention is expressly set forth in the claims at issue on appeal. For example, claim 18 recites in pertinent part:

> administering tunicamycin in an amount effective to inhibit angiogenesis, to a patient in need of such treatment;
> wherein the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight.

In addition, the subject patent application further demonstrates that treatment of angiogenesis by the administration of tunicamycin should be suspended for a period of time. (Id.) As the specification explains, this permits the patient to recover from any adverse reactions and likewise improves patient response. (Specification, p. 49, lines 10-15.) This further aspect of the invention is expressly set forth in the claims at issue on appeal. For example, claim 18 recites in pertinent part:

> wherein the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight, subsequently the administration of the tunicamycin is suspended for a period of about 1 week to 6 months, and subsequently the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight.

VI. Grounds of Rejection to Be Reviewed on Appeal.

As set forth above, the examiner rejected the claims on appeal as obvious in view of Banerjee 1993 and Tiganis 1992.

VII. Argument.

A. Legal Standard.

The examiner bears the burden of establishing a *prima facie* case of obviousness. In re Deuel, 34 U.S.P.Q.2d 1210, 1214 (Fed. Cir. 1995). Only if this burden is met does the burden of coming forward with rebuttal argument or evidence shift to the appellant. Id. To establish a *prima facie* case of obviousness the examiner must provide references which alone or in combination teach each and every element of the claimed invention. In re Fine,

837 F.2d 1071, 1074, 5 U.S.P.Q. 2d 1596, 1598 (Fed. Cir. 1988). When relying upon a combination of references, the teaching or suggestion to modify the references or to make the claimed combination must be found in the prior art, not in appellant's disclosure. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

When the references cited by the examiner fail to establish a *prima facie* case of unpatentability, the rejection is improper and will be overturned. In re Deuel, 34 U.S.P.Q. 2d at 1214. Under these circumstances, the appellant is entitled to a grant of a patent. In re Oetiker, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).

For the reasons set forth below, the examiner's rejections of claims 9, 14 and 18 fail to establish a *prima facie* case of obviousness. When fairly viewed as a whole, the prior art references upon which the examiner relies teach away from applicants' claimed invention.

B. Non-Obviousness.

Each of the claims at issue recites: (1) administering tunicamycin in an amount effective to inhibit angiogenesis to a patient in need of such treatment; and (2) suspending, then re-administering the treatment. (In addition, claims 14 and 18 recite the specific dosage at which tunicamycin is safely administered in humans.)

Banerjee 1993 investigates the link between glycosylation and angiogenesis. In connection with that investigation, Banerjee 1993 discloses various *in vitro* experiments, one of which involves tunicamycin. Banerjee 1993, however, nowhere teaches or even remotely suggests that tunicamycin could be administered to a human patient to inhibit angiogenesis. The examiner does not contend otherwise.

Tiganis 1992 expressly teaches that the administration of tunicamycin *in vivo* would cause damage to brain tissue. Given this expected side effect, Tiganis 1992 in no way

suggests that tunicamycin be administered to a human patient. In fairness, the expectation of brain damage teaches away from the administration of tunicamycin *in vivo*.

Against this background, the subject patent application teaches that tunicamycin can, in fact, be safely administered to a patient. (And, claims 14 and 18 recite the specific dosage.) The claims at issue recite this treatment, which includes the suspension then re-administration of tunicamycin. Since neither of the prior art references relied upon by the examiner contemplated *in vivo* administration of tunicamycin to a patient, neither reference even contemplates the further improvement of suspending then re-admistering the treatment. For these reasons, the examiner has failed to establish a *prima facie* case of obviousness. In fact, when fairly viewed as a whole, Banerjee 1993 and Tiganis 1992 teach away from applicants' claimed invention.

VIII. Claims Appendix.

The claims in this appeal are included as an appendix.

IX. Evidence Appendix.

Applicants do not rely upon any evidence beyond the statements contained in the Specification as originally filed and the prior art references relied upon by the examiner. Accordingly, no evidence appendix is included.

X. Related Proceeding Appendix.

There have not been any other proceedings that would affect or be affected by the Board's decision in this case. Accordingly, no related proceeding appendix is included.

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XI. Conclusion.

For the reason set forth above, appellant respectfully submits that the cited references fail to teach or fairly suggest applicants' claimed invention. In fact the cited references teach away from applicants' claimed invention. Accordingly, the subject claims stand in condition for allowance and the examiner's rejection should be reversed.

Respectfully submitted,

January 2, 2006

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Appendix A

Claim 9: A method for inhibiting angiogenesis, comprising:

administering a nucleoside in an amount effective to inhibit angiogenesis, to a patient in need of such treatment, the nucleoside comprising glucosamine, and wherein the glucosamine comprises at least one tunicamycin and functional derivatives thereof, and wherein the at least one of tunicamycin and factional derivatives thereof is administered for a period of time, subsequently the administration of the at least one of tuniumycin and functional derivatives thereof is suspended for a period of time of at least about 1 week, and subsequently the administration of the at least one of tunicamycin and functional derivatives thereof is resumed.

Claim 14: A method for inhibiting angiogenesis, comprising:

administering a nucleoside in an amount effective to inhibit angiogenesis, to a patient in need of such treatment, the nucleoside comprising glucosamine, wherein the glucosamine comprises at least one of tunicamycin and functional derivatives thereof, and wherein the glucosamine is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight, subsequently the administration of the glucosamine is suspended for a period of about 1 week to 6 months, and subsequently the glucosamine is administered for a period of about 1 week to 6 months at a daily dose of about 5 to 20 mg/kg of body weight.

Claim 18: A method for inhibiting angingenesis, comprising:

administering tunicamycin in an amount effective to inhibit angiogenesis, to a patient in need of such treatment;

wherein the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight, subsequently the administration of the tunicamycin is suspended for a period of about 1 week to 6 months, and subsequently the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight.